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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,379	07/06/2001	Hing C. Wong	44470 C1-CPA-C (71758)	4293

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,379	WONG ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 08/776,084, which is a continuation-in-part of U.S. Application Serial Number 08/382,454, which is a continuation-in-part of U.S. Application Serial Number 08/283,302.

Claims 1-50 have been canceled previously.

New claim 60 has been added.

Claims 51-60 are currently pending and are the subject of examination in the present Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 51, 54 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,260,422 to Clark et al (AB form PTO-1449) in view of McCluskey *et al.* (U1 form PTO-892).

It was previously stated: "The '422 patent discloses MHC Class II fusion complexes comprising an antigen binding site that contain a presented peptide (see column 4, lines 48-55, in particular). The antigen binding site disclosed by '422 patent is the same MHC peptide binding groove taught by the instant application on page 2, lines 4-6. The '422 patent further discloses that the peptide portion in the context of MHC Class II molecule will modulate the activity of a T cell (see column 12, lines 36-45, in particular). The '422 Patent also discloses that peptide and the MHC Class II molecule can be covalently linked (see column 4, lines 58-59, in particular) or that the peptide and MHC molecule may be linked via peptide linkage (see Column 13, 45-47, in particular). The '422 patent further discloses that the MHC Class II molecule may be terminally truncated to delete the transmembrane and cytoplasmic domains (see Figure 1 and Column 6, lines 32-60 and Column 7, lines 1-5, and Column 19, lines 35-45, in particular). The '422 patent also discloses that the presenting peptide may be attached to the N-terminal end of the MHC Class II molecule (see column 13, lines 17-31, in particular). The '422 Patent also discloses that the peptide and MHC molecule may be linked via peptide linkage (see Column 13, 45-47, in particular).

The claimed invention differs from the '422 patent only by the use of MHC Class II fusion complex molecules that are multivalent. However, McCluskey teaches that MHC Class I fusion complexes can be made multivalent by coupling to dextran or agarose beads or by adsorption to polystyrene and that only multivalent preparations stimulate T cells (see abstract, page 1452, left column, second and third paragraphs, and page 1454, left column, last paragraph, in particular).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make multivalent MHC Class II-peptide conjugates using the same methods taught by McCluskey for the purpose of enhancing T cell binding avidity of MHC Class II:peptide fusion molecules."

Applicant's arguments and the declaration of Dr. Peter Rhode filed November 5, 2003 have been fully considered but they are not persuasive. Applicant's arguments are based upon the position presented in the Rhode declaration and the arguments will be addressed as they appear in the remarks section of the amendment filed November 5, 2003.

Applicant argues that the '422 patent does not render the instantly claimed invention obvious because the '422 patent does not teach peptide linker sequences. Applicant argues that the '422 patent merely reports that the MHC molecule and autoimmune antigen may be joined via "a peptide bond" (response, page 7 in particular). However, as pointed out by Applicant, the '422 patent recites that the "autoimmune antigen peptide and the MHC component may be linked via **peptide linkages**." The term "peptide linkages" is understood to mean only that amino acid residues are joined by conventional bonds and is not limited to a single peptide bond between two amino acids. The presently claimed "linker sequence interposed between the presenting peptide and the MHC molecule" is composed of amino acid residues joined to the antigenic peptide, each other, and the MHC molecule via conventional peptide bonds. Further, the recitation of "linkages" in the '422 patent is further evidence that the joining of the MHC molecule and the peptide is not limited to a single "bond" or "linkage," as evidenced by Lehninger (Principles of Biochemistry [1982], pages 111-112 in particular) where it is stated that "[t]wo amino acid molecules can be covalently joined through a substituted amide linkage, termed a *peptide bond*, to yield a *dipeptide*. [...] Three amino acids can be joined by two peptide bonds in a similar manner to form a *tripeptide*" (emphases in original). Accordingly, the term "peptide linkages" is understood in the art to connote more than a single peptide bond. While the '422 patent is silent as to whether there are additional amino acid residues intervening between the MHC molecule and the peptide, the fact remains that in both the '422 patent and in the presently claimed invention, the MHC molecule and the antigenic peptide are joined to one another "via peptide linkages."

Applicant further contends that the '422 patent falls short of rendering the instantly claimed invention obvious because the '422 patent "teaches away" from the use of leader sequences. The Rhode declaration asserts that the addition of a leader sequence assisted in the construction and function of the molecules. While the validity of this assertion of superior results is not questioned, Applicant is reminded that the claim is drawn to the construct itself, not to the method of making it or to the nucleic acid encoding the construct. The claimed invention is drawn to a polypeptide sequence comprising an MHC

class II molecule, a linker sequence and an autoimmune antigenic peptide. The leader sequence is not part of the claimed compound, rather it is part of the initially transcribed protein encoded by the recombinant nucleic acid molecule that is subsequently cleaved off by post-transcriptional processing prior to obtaining the claimed product.

2. Claims 52 and 53 stand rejected under 35 U.S.C. 103(a)) as being unpatentable over U.S. Patent No. 5,260,422 to Clark et al (AB form PTO-1449) in view of McCluskey *et al.* (U1 form PTO-892) as applied to claim 51 above, and further in view of WO 93/10220 (BB form PTO-1449).

It was previously stated: "The '422 patent and McCluskey have been discussed supra. The claimed invention differs from the prior art of record only by linking the multivalent MHC molecules to an immunoglobulin. WO 93/10220 teaches chimeric proteins comprising an MHC component linked to an immunoglobulin constant region component and that the MHC component preferably consists of the extracellular portion of a MHC II protein (see abstract, Figures 2-3, page 3 and Claim 1, in particular). WO 93/120220 teaches that the chimeric proteins can be used to modulate the activity of T cells, such as inducing anergy (see page 9, lines 14-22, and claim 12, in particular). WO 93/10220 also teaches that the chimeric molecules may comprise a single chain MHC molecule linked to immunoglobulin heavy chain. WO 93/10220 also teach multivalent MHC-Ig chimeric protein which comprise MHC molecule that contains a peptide binding groove linked to each of two Ig heavy chain components (see Figure 2, in particular). Therefore it would have been prima *facie obvious* to one with ordinary skill in the art at the time of the invention to modify the MHC-Ig chimeric protein taught by WO 93/10220 by linking the presenting peptide to the multivalent MHC molecule as taught by the combination of the '422 patent and McCluskey with a reasonable expectation that the resulting fusion complex could be used to downregulate the immune response to the presented peptide."

Applicant has merely stated that the '220 document does not correct the deficiencies in the '422 patent and Applicant has not provided further argument regarding the '220 document. Accordingly, this ground of rejection stands as previously stated in light of the further explanation provided in section 1 supra.

3. Claims 55-59 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,260,422 to Clark et al (AB form PTO-1449) in view of McCluskey *et al.* (U1 form PTO-892) as applied to claim 51 above, and further in view of US Patent 5,338,532 to Tomalia et al (A1 form PTO-892)

It was previously stated: "The '422 patent and McCluskey have been discussed supra. The claimed invention differs from the prior art teachings only by use of multivalent MHC fusion molecules chemically linked by a dendrimer particle.

The '532 patent discloses the use of dendrimers as carriers for immuno-potentiating agents to allow for control of the size, shape and surface composition of the conjugate (see column 9, lines 23-54, in particular). The '532 patent further discloses that the dendrimers may be chemically linked to the ligand (see column 13, line 44 through column 16, line 6, in particular). The '532 patent further discloses that use of dendrimers as carriers allows the optimization of antigen presentation to an organism.

Therefore it would have been prima facie obvious to one with skill in the art at the time of the invention to substitute dendrimers for the dextran or agarose beads used by McCluskey in the preparation of multivalent MHC fusion molecule taught by the '422 Patent and McCluskey with the expectation that the multivalent MHC fusion molecule chemically linked by a dendrimer particle would have enhanced T cell binding avidity."

Applicant has merely stated that the '532 patent does not correct the deficiencies in the '422 patent and Applicant has not provided further argument regarding the '220 document. Accordingly, this ground of rejection stands as previously stated in light of the further explanation provided in section 1 supra.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
February 23, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
2/23/04